

University of Groningen

Quality of prescribing in chronic kidney disease and type 2 diabetes

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Appendix 2: Supplemental data chapter 3

File S3.1: Calculation of eligible patients

The number of eligible patients for indicator i was calculated using the formula:

$$n_n = \frac{Z_{\alpha/2}^2 \cdot p_i(100 - p_i)}{d^2}$$

p_i reflects the observed performance score on indicator i , expressed as a percentage.

Z represents the standardised normal variate associated with the 95% confidence interval, which is 1.96.

d reflects the desired level of precision (margin of error) on p_i which was set at 10 percentage points for the medication need and medication choice indicators and at 5 percentage points for safety indicators with outcome $>5\%$ or 1 percentage point for safety indicators with outcome $\leq 5\%$.

Then n_n reflects the number of eligible patients needed to require the set level of precision for the outcome of the indicator.

When the p_i is closer to 100 or closer to 0, less eligible patients are needed, while a p_i closer to 50 will result in a larger number of eligible patients needed.

The minimal number of CKD patients needed for reliable comparison n_{min} is calculated as follows:

$$n_{min} = \frac{n_{tot} \cdot n_n}{n_i}$$

n_{tot} represents the total number of patients in the population, in our case 4,706.

n_n represents the needed number of eligible patients for reliable calculation of the indicator i .

n_i represents the number of eligible patients for indicator i in the population.

File S3.2: Reasons for discarding indicators during the RAM

Eight prescribing quality indicators (PQIs) were discarded during the consensus meeting of the RAND/UCLA Appropriateness Method. The indicator focusing on the preference of angiotensin-converting-enzyme inhibitor/angiotensin-II-receptor-blockers for hypertension (Table 3.1, PQI I) was discarded because the experts decided that this preference is mainly relevant when albuminuria is present. This aspect was covered in indicators 2 and 3. One of the discarded indicators measuring medication need for mineral and bone disorder focused on starting medication treatment (Table 3.1, PQI II). Given the condition that the PQIs should

be defined with routinely collected data, the experts decided that it was not possible to define start of treatment appropriately. The other indicator measuring medication need for mineral and bone disorder was discarded because the experts could not agree on the information needed to assess whether prescribing of vitamin D is indicated (Table 3.1, PQI III). The main reason for discarding all three indicators measuring medication need for anaemia (Table 3.1, PQIs IV, V, VI) was that anaemia is not a specific disorder for patients with chronic kidney disease. The medication safety indicator focusing on adequate monitoring of potassium levels when needed (Table 3.1, PQI VII) was discarded, since it was not possible to define the moment and the frequency of monitoring with routinely collected data. The indicator focusing on prescribing a fixed-combination pill to enhance treatment adherence (Table 3.1, PQI VIII) was discarded because there may be several reasons why patients do not receive such fixed combinations.

Table S3.1: Operationalization final list of prescribing indicators

Overall	Operationalization
Age	Determined on 1 January 2012
Gender	Determined on 1 January 2012
eGFR	CKD-EPI formula using last serum creatinine measurement in 2012
CKD stage 3	Last eGFR ≥ 30 and < 60 ml/min/1.73m ²
CKD stage 4	Last eGFR ≥ 15 and < 30 ml/min/1.73m ²
CKD stage 5	Last eGFR < 15 ml/min/1.73m ²
Renal replacement therapy	Dialysis in 2012 or kidney transplantation ever
Indicators	Operationalization
<i>Treatment of hypertension</i>	
1. The percentage of patients between 18 and 80 years with CKD stages 4-5 and hypertension that is prescribed antihypertensives unless undesirable because of low diastolic blood pressure	<ul style="list-style-type: none"> · Hypertension: <ul style="list-style-type: none"> o systolic blood pressure > 140 mmHg at last measurement in 2012 and/or o diagnosis code for hypertension K86/87 (ICPC) and/or o ≥ 1 prescription for antihypertensives in 2012 · Antihypertensives: ATC codes C02, C03, C07, C08, C09 or combinations (as in C10BX) during the last four months in 2012 · Low diastolic blood pressure: < 70 mmHg at last measurement in 2012

Table S3.1: Operationalization final list of prescribing indicators (continued)

Overall	Operationalization
2a. The percentage of patients between 18 and 80 years with CKD stages 3-5 and macro-albuminuria treated with multiple antihypertensives that is prescribed a combination of an ACE-i or ARB and a diuretic	<ul style="list-style-type: none"> • Macro-albuminuria: ACR>30 mg/mmol at last measurement in 2012 • Multiple antihypertensives: ≥1 prescription for at least 2 different classes (diuretics, beta blocking agents, calcium channel blockers, RAAS inhibitors, other antihypertensives) during the last four months in 2012 • ACE-i/ARB: ATC codes C09A, C09B, C09C, C09D or combinations (as in C10BX) • Diuretic: ATC codes C03A, C03C, C03BA, C03E
2b. The percentage of patients between 18 and 80 years with CKD stages 3-5, micro-albuminuria and diabetes treated with multiple antihypertensives that is prescribed a combination of an ACE-i or ARB and a diuretic	<ul style="list-style-type: none"> • Diabetes: diagnosis code for diabetes T90 (ICPC) • Micro-albuminuria: ACR 3-30 mg/mmol at last measurement in 2012 • Multiple antihypertensives: ≥1 prescription for at least 2 different classes (diuretics, beta blocking agents, calcium channel blockers, RAAS inhibitors, other antihypertensives) during the last four months in 2012 • ACE-i/ARB: ATC codes C09A, C09B, C09C, C09D or combinations (as in C10BX) • Diuretic: ATC codes C03A, C03C, C03BA, C03E
<i>Treatment of albuminuria</i>	
3a. The percentage of patients between 18 and 80 years with CKD stages 3-5 and macro-albuminuria that is prescribed an ACE-i or ARB	<ul style="list-style-type: none"> • Macro-albuminuria: ACR>30 mg/mmol at last measurement in 2012 • ACE-i/ARB: ATC codes C09A, C09B, C09C, C09D or combinations (as in C10BX) during the last four months of 2012
3b. The percentage of patients between 18 and 80 years with CKD stages 3-5, micro-albuminuria and diabetes that is prescribed an ACE-i or ARB	<ul style="list-style-type: none"> • Diabetes: diagnosis code for diabetes T90 (ICPC) • Micro-albuminuria: ACR 3-30 mg/mmol at last measurement in 2012 • ACE-i/ARB: ATC codes C09A, C09B, C09C, C09D or combinations (as in C10BX) during the last four months of 2012
<i>Prescription of statins</i>	
4. The percentage of patients between 50 and 65 years with CKD stages 3-5 that is prescribed a statin	<ul style="list-style-type: none"> • Statin: ATC codes C10AA or combination (as in C10BA, C10BX) during last four months of 2012
<i>Treatment of MBD</i>	
5. The percentage of patients between 18 and 80 years with CKD stages 3-5 and an elevated phosphate level that is prescribed a phosphate binder	<ul style="list-style-type: none"> • Elevated phosphate level: <ul style="list-style-type: none"> o Phosphate level: >1.49 mmol/l at last measurement in 2012 and/or o ≥1 prescription for phosphate binder during last four months of 2012 • Phosphate binder: ATC codes A12AA04, A12AA12, V03AE02, V03AE03, V03AE04, A02AB01

Table S3.1: Operationalization final list of prescribing indicators (continued)

Overall	Operationalization
6. The percentage of patients between 18 and 80 with CKD stages 3-5 treated with phosphate binders and with an elevated calcium level that is prescribed a non-calcium-containing phosphate binder	<ul style="list-style-type: none"> · Elevated calcium level: >2.54 mmol/l at last measurement in 2012 · Phosphate binder: ATC codes A12AA04, A12AA12, V03AE02, V03AE03, V03AE04, A02AB01 during last four months of 2012 · Non-calcium containing phosphate binder: ATC codes V03AE02, V03AE03, A02AB01 during last four months of 2012
7. The percentage of patients between 18 and 80 with CKD stages 3-5 treated with phosphate binders and with a low calcium level that is prescribed a calcium-containing phosphate binder	<ul style="list-style-type: none"> · Low calcium level: <2.10 mmol/l at last measurement in 2012 · Phosphate binder: ATC codes A12AA04, A12AA12, V03AE02, V03AE03, V03AE04, A02AB01 during last four months of 2012 · Calcium containing phosphate binder: ATC codes A12AA04, A12AA12, V03AE04 during last four months of 2012
<i>Medication safety</i>	
8. The percentage of patients 18 years or older with CKD stages 3-5 treated with RAAS inhibitors that is prescribed at least two RAAS inhibitors simultaneously (dual RAAS blockade)	<ul style="list-style-type: none"> · RAAS inhibitors simultaneously: at least 2 of the ATC codes C09A, C09B, C09C, C09D, C09X or combination (as in C10BX) during last four months 2012
9. The percentage of patients 18 years or older with CKD stages 3-5 and an elevated calcium level that is prescribed active vitamin D	<ul style="list-style-type: none"> · Elevated calcium level: >2.54 mmol/l at last measurement in 2012 · Active vitamin D: ATC codes A11CC02, A11CC03, A11CC04, H05BX02 during last four months of 2012
10. The percentage of patients 18 years or older with CKD stages 3-5 and an haemoglobin level above target that is prescribed an ESA	<ul style="list-style-type: none"> · Haemoglobin level: $\geq 7,5$ mmol/l at last measurement in 2012 · ESA: ATC codes B03XA01, B03XA02 during last four months of 2012
11. The percentage of patients 18 years or older with eGFR <30ml/min/1.73m ² that is prescribed an NSAID	<ul style="list-style-type: none"> · NSAID: ATC codes M01A, M01BA and B01AC06, B01AC08, B01AC30, B01AC56, N02BA01, N02BA15, N02BA51, N02BA65 in dose >160 mg/day during last four months of 2012
12. The percentage of patients 18 years or older with eGFR <30 ml/min/1.73m ² and diabetes that is prescribed metformin	<ul style="list-style-type: none"> · Diabetes: diagnosis code for diabetes T90 (ICPC) · Metformine: ATC codes A10BA02 or combination (as in A10BD) during last four months of 2012
13. The percentage of patients 18 years or older with eGFR <50 ml/min/1.73m ² treated with digoxin that is prescribed high dose digoxin	<ul style="list-style-type: none"> · Digoxin: ATC code C01AA05 · High dose digoxin: ATC code C01AA05 in dose >0.125 mg/day during last four months of 2012

Table S3.1: Operationalization final list of prescribing indicators (continued)

Overall	Operationalization
14. The percentage of patients 18 years or older with CKD stages 3-5 and that is prescribed a combination of NSAIDs, RAAS inhibitors and diuretics	<ul style="list-style-type: none"> · Combination of NSAIDs, RAAS inhibitors and diuretics during the last four months of 2012 o NSAIDs: ATC codes M01A, M01BA and B01AC06, B01AC08, B01AC30, B01AC56, N02BA01, N02BA15, N02BA51, N02BA65 in dose > 160 mg/day o RAAS inhibitors: ATC codes C09 and combinations (as in C10BX) o Diuretics: ATC codes C03

eGFR: estimated glomerular filtration rate; CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration; CKD: chronic kidney disease; ICPC: International Classification of Primary Care; ATC: Anatomical Therapeutic Chemical Classification System; ACE-i: angiotensin-converting-enzyme inhibitor; ARB: angiotensin-II-receptor-blocker; ACR: albumin/creatinine ratio; RAAS: renin-angiotensin-aldosterone system; MBD: mineral and bone disease; ESA: erythropoiesis-stimulating agent; NSAID: non-steroidal anti-inflammatory drug, including salicylic acid and derivatives.